REMARKS

In view of the amendments and remarks herein, the Examiner is requested to allow Claims 1-4, 8-19, 21-24 and 34-39, the only claims pending and under examination in this application.

Claims 1, 11 and 24 have been amended to correct minor typographical errors. Claims 30 and 31 have been cancelled.

Claims 34-39 have been added. Support for these new claims is found throughout the specification and claims as originally filed, for example at page 22-23, ¶¶ [0094]-[0095]; page 32, ¶ [0117]; page 33, ¶¶ [0119]-[0120]. As such, no new matter has been added.

As no new matter has been added by way of the above amendments, entry thereof by the Examiner is respectfully requested.

Claim Rejections – 35 U.S.C. § 103

Claims 1-4, 8-19 and 21-24 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Webb et al. (GB 2355716) in view of Blanchard (U.S. Patent No. 6,419,883).

In order to meet its burden in establishing a rejection under 35 U.S.C. §103, the Office must first demonstrate that a prior art reference, or references when combined, teach or suggest all claim elements. *See e.g., KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007); *Pharmastem Therapeutics v. Viacell et al.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007); MPEP § 2143(A)(1). In addition to demonstrating that all the elements were known in the prior art, the Office must also articulate a reason for combining the elements. *See e.g., KSR*, 127 S.Ct. at 1741; *Omegaflex, Inc. v. Parker-Hannifin Corp.*, 243 Fed. Appx. 592, 595-596 (Fed. Cir. 2007) (citing *KSR*). Further, the Supreme Court in *KSR* also stated that that "a court *must* ask whether the improvement is more than the predictable use of prior art elements according to their established functions." *KSR*, 127 S.Ct. at 1740 (emphasis added). As such, in addition to showing that all elements of a claim were known in the prior

art and that one of skill had a reason to combine them, the Office must also provide evidence that the combination would be a predicted success.

The rejected claims are directed to methods of fabricating a chemical array of biopolymeric ligands and include the element of "determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition".

The Examiner alleges that Webb substantially discloses the instantly claimed invention. Office Action, pg. 3-4, section 4, ¶ 3 (citing Webb, FIGS. 16-19, and pg. 30-35). However, the Examiner concedes that Webb "is silent regarding the monomer solution." Office Action, pg. 3-4, section 4, ¶ 3. Thus, the Examiner cites to Blanchard and alleges that Blanchard discloses that "the most preferred monomer for in situ synthesis is a phosphoramidite". Office Action pg. 4, lines 1-3 (citing Blanchard, col. 14, lines 42-45).

The Applicants respectfully disagree. Webb actually discloses that "The method includes examining at least one operating parameter of the apparatus for an error from a nominal value . . . When an error is detected, a corrected drive pattern different from the target drive pattern is derived, based on the error". Webb, pg. 8, lines 14-15. In addition, Webb discloses as follows:

> **The at least one operating parameter can be selected from one or more of any parameter which would affect the actual array pattern deposited. For example, these may include: a position of the dispensing head or any other dispensing apparatus component; the accuracy of an encoder used to detect the position of the dispensing head or the substrate; the accuracy in an ability of the transport system to move the substrate or head to an expected location in response to a command (for example, deviation of actual movement from a corresponding nominal axis of movement); or the position of a position of a nozzle in a multiple nozzle dispensing head**

However, nowhere does Webb disclose or suggest the element of "determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition". Blanchard was cited solely for its alleged disclosure of using phosphoramidites for in situ synthesis. Thus, Blanchard fails to remedy the deficiencies in Webb. As such, the cited combination of Webb and Blanchard fails to disclose or suggest all the elements of the Applicants' claimed invention, and the Applicants respectfully request withdrawal of this rejection.

Claims 1-4, 8-19 and 21-24 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Blanchard (U.S. Patent No. 6,419,883) in view of Hirota et al. (U.S. Patent No. 6,753,144).

As indicated above, the rejected claims are directed to methods of fabricating a chemical array of biopolymeric ligands and include the element of "determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition".

In making the instant rejection, the Examiner asserts that Blanchard discloses "determining a chemical layout based on composition to be produced, i.e. 'the name of an oligo specification files storing the geometry of the desired patterns to be deposited in a particular wafer'". Office Action, pg. 6, section 5, ¶ 2. However, the Examiner concedes that "Blanchard differs from the claimed invention in that the reference does not specifically teach modulating the deposition head to dispense differing volumes to thereby produce the differing sized features." Office Action, pg. 6-7, bridging paragraph. Thus, the Examiner attempts to remedy the deficiencies in Blanchard by citing Hirota.

The Applicants respectfully disagree and contend that a *prima facie* case of obviousness has not been established because the cited combination of Blanchard and Hirota fails to teach all the elements of the rejected claims.

The disclosure of Blanchard "relates to a microdroplet of a solution, the solution comprising a high surface tension solvent having a boiling point of about 150° C. or above, a surface tension of about 30 dynes/cm or above, and a viscosity of about 0.015 g/(cm)(sec) or above." Blanchard, col. 5, lines 56-61. In describing the properties of the microdroplets, Blanchard indicates that "These properties are particularly desirable when the amount of solute, e.g., a reactive chemical species, that is to be dispensed as a microdroplet solution, should preferably be uniform from microdroplet to microdroplet", and that "This property is particularly important when the dispensed microdroplets are to be deposited in closely packed arrays of uniformly shaped microdots that cannot overlap." Blanchard, col. 7, lines 22-26 and lines 37-40. Thus, Blanchard discloses that "microdroplets are to be deposited in closely packed arrays of uniformly shaped microdots". As such, Blanchard does not disclose or suggest the Applicants' claimed element of "determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition", and in fact teaches away from this element.

Furthermore, the Examiner cites to Blanchard and alleges that "Blanchard further teaches the resulting features have differing sizes. Office Action, pg. 6, section 5, ¶ 2 (citing Blanchard, col. 9, lines 44-45).

The Applicants respectfully disagree. Blanchard actually discloses that "surface tension wells can constrain each microdot, and prevent adjacent microdots from overlapping or merging with each other. According to the invention, methods have been developed that produce an array of microdots that are in the form of circular wells." Blanchard, col. 9, lines 37-42. See also FIG. 1a of Blanchard, reproduced below:

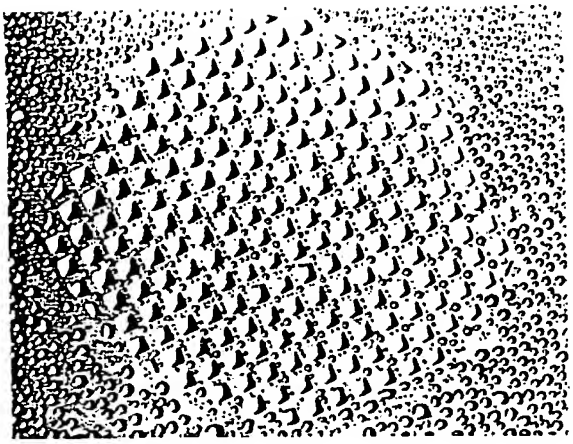

Fig. 1a

Thus, in light of the above, Blanchard is not teaching spots of different sizes *on a single array*, as suggested by the Examiner, but rather that different arrays may have different sized spots. In other words, each array has a uniform spot size, but when compared to other arrays, each array may have different size spots from another. Consequently, Blanchard fails to disclose or suggest the Applicants' claimed element of "determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition".

In addition, the Examiner contends that "the waveform modulation to dispense differing volumes and produce spots of differing sizes was well known and routinely practiced in the art at the time the claimed invention was made as taught by Hirota et al." Office Action, pg. 7, lines 3-5 (citing Hirota, col.12). However, in describing methods of producing a DNA microarray, Hirota actually discloses as follows:

> During this process, when the supply position is appropriately changed, the droplets of the supplied sample solution are combined (integrated) on the base plate **10** to form the sample solution having one spot diameter. Further, it is possible to realize a uniform spot diameter formed on the base plate **10** by controlling the number of supply operations, the supply position, and the amount of one time supply, depending on the type of the sample solution to be supplied.

Hirota, col. 12, lines 36-44. Thus, Hirota discloses that the droplets on the vase plate have "a uniform spot diameter". Consequently, similar to Blanchard above, Hirota does not disclose or suggest the Applicants' claimed element of determining a chemical array layout in which each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition". Therefore, the cited combination of Blanchard and Hirota does not disclose or suggest all the elements of the Applicants' claims, and this rejection may be withdrawn.

Moreover, as disclosed in the Applicants' specification, "the ability to control the size of each feature of an array is provided by the subject methods. That is, the subject methods provide the ability to customize the chemistry or feature size for each feature (e.g., for each synthesized base) on a per surface bound ligand, e.g., probe, basis (as opposed to a per print swath column or per entire substrate or entire substrate layer basis)." Specification, pg. 15-16, ¶ [0067]. As such, the rejected claims are directed to a method of *in situ* array fabrication. This *in situ* method is captured in the claims, for example in the elements that: "each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition"; "said fabricating comprises modulating an applied activation signal for each ejector of said at least one deposition head to produce said features"; and 'said method further comprises transmitting said feature sizes to said processor, whereby said processor performs said modulating based on said feature sizes".

As indicated above, the Examiner concedes that Blanchard fails to teach modulating the deposition head to dispense differing volumes to thereby produce the differing sized features. As such, Blanchard fails to disclose or suggest a method for *in situ* array fabrication, as claimed by the Applicants.

In attempting to remedy the deficiencies of Blanchard, the Examiner cites to Hirota and alleges that "the waveform modulation to dispense differing volumes and produce spots of differing sizes was well known and routinely practiced in the art at the time the claimed invention was made as taught by Hirota et al." Office Action, pg. 7, lines 3-5 (citing Hirota, col.12).

The Applicants respectfully disagree. Hirota actually discloses that producing a DNA microarray includes "a sample preparation step **S2** of preparing the sample solution containing DNA fragment, and a supply step **S3** of supplying the obtained sample solution onto the base plate **10**." Hirota, col. 6, lines 43-46, and Figs. 2-3. In addition, Hirota discloses that the DNA fragments are "PCR product[s] amplified by using a known PCR machine". Hirota, col. 7, lines 8-10. Thus, Hirota only discloses producing a DNA microarray by affixing DNA fragments obtained by PCR onto a base plate, and in no way discloses or suggests a method for *in situ* array fabrication, as claimed by the Applicants.

Consequently, nowhere does Blanchard or Hirota disclose or suggest the Applicants' claimed method of *in situ* array fabrication, which is captured in the claim elements that: "each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition"; "said fabricating comprises modulating an applied activation signal for each ejector of said at least one deposition head to produce said features"; and 'said method further comprises transmitting said feature sizes to said processor, whereby said processor performs said modulating based on said feature sizes".

In view of the above, a *prima facie* case of obviousness cannot be maintained because the cited combination of Blanchard and Hirota fails to teach or suggest all the elements of the rejected claims. Consequently, the Applicants respectfully request that the rejection of Claims 1-4, 8-19 and 21-24 under 35 U.S.C. § 103(a) be withdrawn.

Alternatively, the Examiner alleges that "it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the deposition of Hirota by using the phosphoramidite solution and in situ synthesis of Blanchard."

In making this alternative rejection, the Examiner asserts that "Hirota et al disclose a method of fabricating an array of biopolymers with different feature sizes

(Fig. 14), the method comprising modulating a waveform to at least one orifice ejector (discharge port, #54, Fig. 6) to dispense volumes of fluid from the orifice wherein the volume is based on modulated waveform (Column 11, lines 62-Column 12, line 45, Fig. 9)." Office Action, pg. 7, last paragraph. However, the Examiner acknowledges that Hirota is deficient in that it fails to teach or suggest use of a layout and processor. Office Action, pg. 8, ¶ 1. Thus, the Examiner relies upon Blanchard to remedy the deficiencies of Hirota.

The Applicants respectfully disagree. As discussed above, both Hirota and Blanchard are fatally deficient in that they both fail to disclose or suggest the Applicants' claimed method of *in situ* array fabrication, which is captured in the claim elements that: "each feature in said chemical array layout has a feature size that is chosen based on its biopolymeric ligand composition"; "said fabricating comprises modulating an applied activation signal for each ejector of said at least one deposition head to produce said features"; and 'said method further comprises transmitting said feature sizes to said processor, whereby said processor performs said modulating based on said feature sizes".

Consequently, a *prima facie* case of obviousness cannot be maintained because the cited combination does not teach or suggest all the elements of the rejected claims. Therefore, the Applicants respectfully request that the rejection of Claims 1-4, 8-19 and 21-24 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

In view of the amendments and remarks above, Applicant(s) respectfully submit(s) that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret E. Field, (650) 327-3400.

The Commissioner is hereby authorized to charge any additional fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-1078, order number 10031095-1.

Respectfully submitted,

Date: October 7, 2008

By: /Rudy J. Ng, Reg. No. 56,741/
Rudy J. Ng
Registration No. 56,741

Date: October 7, 2008

By: /David C. Scherer, Reg. No. 56,993/
David C. Scherer, Ph.D.
Registration No. 56,993

AGILENT TECHNOLOGIES, INC.
Legal Department, DL429
Intellectual Property Administration
P.O. Box 7599
Loveland, CO 80537-0599

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